E2 Cont (f) any combination of (a)-(e).

REMARKS

Claims 3-7, 9, 11-13 and 16-20 presently appear in this case. Claims 9, 11-13 and 16-20 have been withdrawn from consideration to the extent that they read on non-elected inventions. No claims have been allowed. The official action of March 27, 2002, has now been carefully studied. Reconsideration and allowance are hereby respectfully urged.

Briefly, the present invention relates to a method of ameliorating the degenerative effects of injury or disease on the central nervous system or peripheral nervous system by preventing or inhibiting axonal degeneration and/or promoting nerve regeneration, with the proviso that the disease is other than an autoimmune disease or a neoplasia. It has been discovered that NS-specific anti-self-activated T cells accumulate at a site of injury or disease of the CNS or PNS and have a neuroprotective effect. Thus, the method comprises the administration of such T cells, or antigens or peptides which activate T cells *in vivo* to produce such a population of T cells, or a nucleotide sequence which encodes such a NS-specific antigen or peptide for the purpose of activating such T cells.

The examiner has repeated the restriction requirement, but concluded that, upon the determination of allowable subject matter, the examiner would reconsider rejoinder depending on the terms of the claims. Applicants reserve the right to petition from the requirement for restriction within the time period set in 37 C.F.R. §1.144.

Claims 3-7, 9, 13 and 16-20 have been objected to under 37 C.F.R. §1.75(c) as being drawn to non-elected subject matter and, thus, to multiple patently distinct inventions. This rejection is respectfully traversed.

The examiner cites MPEP §803.02 in support of this objection. However, the examiner ignores the first paragraph of this section of the MPEP, which reads:

> If members of the Markush group are sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden, the examiner must examine all the members of the Markush group and the claim on the merits, even though they are directed to independent and distinct inventions. In such a case, the examiner will not follow the procedure described below and will not require restriction.

As the examiner has only identified two groups, they should both be examined regardless of whether or not they are independent and distinct. The examiner has already indicated that she would reconsider examining all the groups once

allowable subject matter is found. Thus, it is requested that this objection be held in abeyance until that time.

Reference is also made further in MPEP §803.02, where it states:

> On the other hand, should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim will be extended.

Regardless of whether or not Group I and Group II as designated by the examiner are independent and distinct, they are not so diverse as to create an improper Markush group. Thus, both species should be examined once one is found allowable. Reconsideration and withdrawal of this objection or holding it in abeyance until allowable subject matter is found in the case are respectfully urged.

Claims 3-7, 9, 13 and 16-20 have been rejected under 35 U.S.C. §112, first paragraph, new matter. The examiner states that applicants have amended claim 16 to recite "wherein said injury or disease is other than an autoimmune disease or a neoplasm", yet the specification does not appear to support such a recitation. This rejection is respectfully traversed.

The examiner's attention is invited to page 24 of the specification, lines 14-19, which states:

> In a preferred embodiment, the NS-specific antiself activated T-cells, the NS-specific

> antigens, peptides derived therefrom, derivatives thereof or the nucleotides encoding said antigens, or peptides or any combination thereof of the present invention are used to treat diseases or disorders which are not autoimmune diseases or neoplasias. [emphasis added]

In view of this disclosure in the specification, claim 16, and those claims which depend therefrom, contain no new matter. Reconsideration and withdrawal of this rejection are respectfully urged.

Claims 3-7, 9, 13 and 16-20 have been rejected under 35 U.S.C. §112, first paragraph, written description. The examiner states that the claims have been amended from the generic of any disease or injury to the sub-generic of diseases and injuries "other than an autoimmune disease or a neoplasm." The examiner states that applicants were not in possession of such a sub-generic class. This rejection is respectfully traversed.

As indicated above, the specification does indicate that a preferred embodiment of the invention does not involve treating diseases or disorders which are autoimmune diseases or neoplasias. Thus, it is clear that applicants were in possession of this sub-genus and it is supported by the specification. In any event, a 35 U.S.C. §112, first paragraph, written description rejection is one and the same as a 35 U.S.C. §112, new matter rejection. See MPEP §2163.06.

Reconsideration and withdrawal of this rejection for the same reason as discussed above with respect to the new matter rejection are, therefore, respectfully urged.

Claims 4-7, 9, 13 and 16-20 have been rejected under 35 U.S.C. §112, enablement. The examiner states that, while the specification is enabling for ameliorating degenerative effects consistent with Example 9 in crush injury of rat optic nerve, ischemia and in injuries associated with ischemia, as claimed in claim 3, it does not reasonably provide enablement for the broad, but sub-generic recitation of ameliorating the degenerative effects of injury or disease other than autoimmune disease or a neoplasm. The examiner stated that there is no enablement for alternative diseases not largely associated with crush trauma or ischemia, such as glaucoma and Alzheimer's Disease, hearing loss or mental retardation. This rejection is respectfully traversed.

The preamble of claim 16 has now been amended to further clarify the types of effects that the present invention is intended to treat. It now provides that the method is for "ameliorating the effects of injury on the central or peripheral nervous system or the degenerative effects in the grey and/or white matter caused by a disease that results in a degenerative process." This language is supported by the paragraph bridging pages 23 and 24 of the

present specification. The claim goes on to state that such amelioration is accomplished "by preventing or inhibiting axonal degeneration and/or promoting nerve regeneration." The crush tests show that the present invention is efficacious for preventing or inhibiting axonal degeneration and/or promoting nerve regeneration. Accordingly, it is not incredible to believe that axonal degeneration caused by the degenerative effects in the grey and/or white matter caused by a disease that results in a degenerative process cannot be inhibited or that nerve regeneration cannot be promoted in such an instance. It is not understood that hearing impairment or color blindness, as suggested by the examiner, is necessarily a degenerative effect on the grey and/or white matter caused by a disease that results in a degenerative process.

The examiner further states that the art is unpredictable in the requirements necessary for effects sufficient to restore function. However, the present claims do not require that function be restored. It only requires that the effects of injury on the central or peripheral nervous system or the degenerative effects in the grey and/or white matter caused by a disease that results in a degenerative process can be ameliorated. The term "ameliorating" merely means improving the situation. It does not require restoration of function in order to qualify as

amelioration. As long as there is any improvement in the degenerative effects, this is an amelioration, and the claim is met and a real world utility is established. This would not be deemed incredible to those of ordinary skill in the art, particularly in light of the enablement which the examiner concedes with respect to the effects of crush injury on the central or peripheral nervous system. Accordingly, reconsideration and withdrawal of this rejection are respectfully urged.

Claims 3-7, 9, 13 and 16-20 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite as the claim structure recites administering to a human having a disease that encompasses all injuries and diseases with the exception of when the injury or disease is an autoimmune disease or a neoplasm. The examiner states that the specification fails to distinguish the metes and bounds of the injuries or diseases included or excluded from the claim, particularly with the specific inclusion of diabetic neuropathy and glaucoma which can be a degenerative effect of diabetes. This rejection is respectfully traversed.

Diabetic neuropathy is not an autoimmune disease. It is not caused by an attack of the immune system on the self. It is a non-autoimmune disease which is separate from diabetes, notwithstanding the fact that it is found in

diabetic patients and may be a side effect of diabetes. It is quite beneficial to diabetic patients to have the neuropathy or glaucoma which is secondary to their diabetes be ameliorated, even if the treatment has no effect on the diabetes *per se*. The examiner's attention is also invited to the statement at page 23, line 24, to page 24, line 13, that the specifically listed diseases, such as "diabetic neuropathy", are "not recognized by those of reasonable skill in the art as being autoimmune diseases or disorders". Reconsideration and withdrawal of this rejection are therefore respectfully urged.

Claims 3, 5-7, 9, 13, 16, 17, 19 and 20 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Becker and The Merck manual. This rejection is respectfully traversed.

Becker is dated September 1997. The present application is a CIP of an international application filed on July 21, 1998. Therefore, Becker is not available as a reference under 35 U.S.C. §102(b)/103, but only under 35 U.S.C. §102(a)/103. Thus, Becker is only available as a reference if it was published before applicants' date of invention. The PCT application, of which the present application is a CIP, was originally filed claiming priority to two Israeli applications, IL 121349, filed July 21, 1997,

and IL 124550, filed May 19, 1998. While the priority claim to the first application was withdrawn (erroneously) and the PCT rules did not allow it to be reinstated, nevertheless, the rules applicable to this CIP application do not prevent applicants from again claiming this priority application in the present case. Accordingly, priority of IL 121349, filed July 21, 1997, is hereby claimed. A photocopy of the certified copy of this application is attached hereto. A certified copy will be filed in due course. As applicants are entitled to the priority date of May 19, 1997, Becker is not available as a reference. The examiner does not contend that Merck alone makes the present invention obvious. Reconsideration and withdrawal of this rejection are, therefore, respectfully urged.

It is submitted that all the claims now present in the case clearly define over all the publications of record which are available as prior art and fully comply with 35 U.S.C. §112. Reconsideration and allowance are, therefore, earnestly solicited.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The

attached page is captioned "Version with markings to show changes made".

Respectfully submitted,

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Version with Markings to Show Changes Made

Claims 4 and 16 have been amended as follows:

4 (~~Thrice~~Four Times-Amended). A method in accordance with claim 16, wherein said method is for ameliorating the degenerative effects on the central nervous system or the peripheral nervous system which are a result of a disease selected from the group consisting of diabetic neuropathy, senile dementia, Alzheimer's disease, Parkinson's Disease, facial nerve (Bell's) palsy, glaucoma, Huntington's chorea, amyotrophic lateral sclerosis, non-arteritic optic neuropathy, and vitamin deficiency, and wherein said human is one having such a disease.

16 (~~Twice~~Thrice-amended). A method of ameliorating the ~~degenerative~~ effects of injury on the central or peripheral nervous system or the degenerative effects in the grey and/or white matter caused by a disease ~~on the central nervous system or peripheral nervous system~~that results in a degenerative process, said disease being other than an autoimmune disease or a neoplasia, by preventing or inhibiting axonal degeneration and/or promoting nerve regeneration, ~~wherein said injury or disease is other than an autoimmune disease or a neoplasm,~~ comprising administering to a human having such an injury or disease an effective amount for

neuroprotection of a composition comprising an agent selected from the group consisting of:

(a) non-recombinant, NS-specific antiself activated T-cells;

(b) a NS-specific antigen or a derivative thereof;

(c) a peptide derived from a NS-specific antigen or a derivative thereof;

(d) a nucleotide sequence encoding a NS-specific antigen;

(e) a nucleotide sequence encoding a peptide derived from a NS-specific antigen; and

(f) any combination of (a)-(e).